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RESEARCH REPORT

Learning Health Systems

Learning healthcare systems in cardiology: A qualitative interview study on ethical dilemmas of a learning healthcare system

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Abstract

Background: Implementation of an LHS in cardiology departments presents itself with ethical challenges, including ethical review and informed consent. In this qualitative study, we investigated stakeholders' attitudes toward ethical issues regarding the implementation of an LHS in the cardiology department.

Methods: We conducted a qualitative study using 35 semi-structured interviews and 5 focus group interviews with 34 individuals. We interviewed cardiologists, research nurses, cardiovascular patients, ethicists, health lawyers, epidemiologists/statisticians and insurance spokespersons.

Results: Respondents identified different ethical obstacles for the implementation of an LHS within the cardiology department. These obstacles were mainly on ethical oversight in LHSs; in particular, informed con sent and data ownership were discussed. In addition, respondents reported on the role of patients in LHS. Respondents described the LHS as a possibility for patients to engage in both research and care. While the LHS can promote patient engagement, patients might also be reduced to their data and are therefore at risk, according to respondents.

Conclusions: Views on the ethical dilemmas of a LHSs within cardiology are diverse. Similar to the literary debate on oversight, there are different views on how ethical oversight should be regulated. This study adds to the literary debate on oversight by highlighting that patients wish to be informed about the learning activities within the LHS they participate in, and that they wish to actively contribute by sharing their data and identifying learning goals, provided that informed consent is obtained.

KEYWORDS
cardiology, ethics, learning healthcare system, qualitative research

1 | INTRODUCTION

LHSs are defined as healthcare systems in which "science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the delivery process and new knowledge captured as an integral by-product of the delivery experience."[1] Thus, in LHSs, routinely collected patient data are used to create a continuous feedback loop between research and healthcare. By combining insights from research and clinical care, the effectiveness of clinical care methods that are already implemented, but for which the substantiating evidence (eg, regarding safety) is suboptimal, can be investigated.[1,2] In addition, LHSs could provide a platform for studying innovations in clinical care, such as new medical techniques.[1,3] Another potential advantage of LHSs is that using an LHS could help to reduce healthcare costs and to lower administrative burdens for doctors and researchers.[1,3,4] Lastly, LHSs may function as a platform for applying and investigating practices such as e-health.[1,3,5] E-health is defined by the World Health Organization as the use of information and communication technologies (ICT) for health.[6] There is no one-size-fits-all approach when it comes to implementing LHSs. In literature, different practices are described as LHS; these practices vary in the methods they employ and their goals.[7] While some LHSs might, for instance, use large databases for observational research with routinely collected data, others might aim to implement randomized controlled trails (RCTs) in clinical care.[7]

Despite the advantages, LHSs present their challenges.[7] For instance, for an LHS to succeed, participation with the LHS is needed from all stakeholders. Also, informed consent models for participants and ethical oversight may need to be specifically tailored to the LHS.[8,9] It is currently unclear how these challenges with LHSs can be approached most effectively. If cardiology wants to become a "learning laboratory" and expand knowledge to other fields of medicine,[2] ethical challenges must be addressed.

The present study aims to collect perceived ethical issues regarding the implementation of an LHS and to investigate stakeholders' attitudes toward the concept of the LHS, ethical review and informed consent.

To the best of our knowledge, this type of qualitative research is new. Weinfurt and colleagues have performed a survey related to pragmatic trials with similar issues, and ethical obligations for LHS as identified by Faden and colleagues have been deepened by collecting experiences.[10,11]

We chose the cardiology department as our research object because of the combination of the use of routinely collected patient data to create a continuous feedback loop between research and care, and the continuous technological innovations. In 2017, the American Heart Association argued that cardiology might be the ideal "learning laboratory" for a Learning Healthcare System (LHS).[2]

2 | METHODS

2.1 | Study design

From mid 2019 to end 2020, we conducted a qualitative study, using semi-structured interviews and five focus groups, to explore stakeholders' views on the implementation of an LHS in a cardiology department and to investigate stakeholders' attitudes toward the concept of the LHS, ethical review and informed consent. We conducted this study in the field of cardiology because inherent to this field are rapid changes in medical technology and the increasing use of patient data for research and care optimization.

2.2 | Sample and setting

We used purposeful sampling to select members from eight stakeholder groups: patients, cardiologists, (research) nurses, insurance spokespersons, policy makers, health lawyers, methodologists (epidemiologists/statisticians) and ethicists. Cardiovascular patients were approached via their cardiologist. We also asked members of the Dutch patient association of heart patients (Harteraad, https://harteraad.nl/). Cardiologists and (research) nurses were approached via several cardiology departments from different hospitals. The insurance spokespersons were approached via cardiologists. Insurance spokespersons were senior advisors on the funding of new healthcare innovations. Policy makers were linked to a cardiology department and were responsible for the implementation of new interventions and paradigms in healthcare. Ethicists, lawyers and methodologists were approached via ethical review boards. All ethical review boards in the Netherlands were contacted. An overview of the interviewed stakeholders can be found in Table 1. Respondents differed in how knowledgeable they were on the concept of an LHS. Whereas some respondents reported having professional experience with the concept, others had yet to encounter the concept in their practices.

2.2.1 | Focus groups

First, five 90-minute stakeholder focus groups were organized. Two were performed with five cardiovascular patients each and three focus groups were performed with eight stakeholders each, including two cardiologists, a research nurse, insurance spoke person/policy maker, an ethicist, a patient, a methodologist, and a health lawyer. Focus groups were in Dutch and designed to[1] explore the knowledge of stakeholders on the concept of an LHS,[2] discuss the use of various informed consent models within an LHS, and[3] reflect on ethical oversight within an LHS. Respondents were asked to indicate to what extent they were familiar with LHSs and to give their opinion on the concept of an LHS. The following working definition of an LHS was given: "a system in which science, informatics, incentives, and culture are aligned for continuous improvement and innovation, with best practices seamlessly embedded in the delivery process and new knowledge captured as an integral by-product of the delivery experience."

TABLE 1 Characteristics of respondents in a qualitative interview study on dilemmas of a learning healthcare system.

Type of respondents	Total number of respondents
Patients	14
Research nurses	8
Cardiologists	18
Methodologists	10
Ethicists	11
Health lawyers	9
Policy makers	6
Focus group interviews	**Total of respondents**
Patients	14
Research nurses	3
Cardiologists	8
Methodologists	4
Ethicists	4
Health lawyers	4
Policy makers	4
Individual interviews	**Total of respondents**
Patients	0
Research nurses	5
Cardiologists	10
Methodologists	5
Ethicists	6
Health lawyers	5
Policy makers	4
Involvement	**Total of respondents**
Cardiology department	43
Ethical review board	27
Cardiology and ethical review board	6

TABLE 2 The Box & The Utrecht Cardiovascular Cohort—examples of a learning healthcare system.

The Box

In 2016, the Leiden University Medical Center (LUMC) started a randomized controlled trial to determine if frequent monitoring using smartphone-compatible wearable technologies and replacement of out patient clinic visits by electronic visits might improve clinical effectiveness and patient satisfaction of care.[12] Cardiovascular patients were, when they gave their consent and met the selection criteria, randomly divided in two groups. The test groups were given a box with home measurement instruments consisting of; a blood pressure monitor, a weight scale, heart rhythm measuring equipment, a watch with pedometer. After a year of follow up, the patients who received The Box and had electronic visits had equally regulated blood pressure, and the percentages of patient satisfaction and hospitalizations were similar to standard care.[12] After this successful study, "The Box" was provided to all patients in cardiovascular care paths in the LUMC to monitor their health and for example, help control their blood pressure, detect arrhythymias or monitor recovery after surgery. Patients measure vital parameters at home, these data are sent to the LUMC and used to optimize their healthcare. Before patients visit the LUMC or consult with their caregiver at home via a webcam, the data patients have gathered are used to create a more complete image of the patient. Measurements will be discussed during the consult. On top of individual healthcare, these home measurements are used for research purposes. This involves the improvement of quality of care and scientific research within the LUMC. Since patient data is used to provide for individual care as well as (scientific) research and quality improvement, The Box is identified as LHS by the researchers.

Utrecht Cardiovascular Cohort

In 2014, the Utrecht Cardiovascular Cohort (UCC), started with the implicit and later explicit wish to become an LHS. This cohort study consists of patients in the University Medical Center Utrecht who suffers from any kind of (risk of) cardiovascular disease. Patients are asked to participate in the cohort after receiving information at home and to give explicit informed consent at their first consult. The UCC aims to improve the quality of electronic health records by unifying the department's register protocols, provide feedback to physicians on quality of care, generate new evidence on development and occurrence of disease, predication of development or presence of disease and therapeutic possibilities including; efficacy, safety and cost-effectiveness for cardiovascular disease. The UCC consists of[1] collection of routine care data about cardiovascular risk factor assessment,[2] linkage to other health data sources and[3] a biobank. In the future, the UCC hopes to provide feedback to patients on their own health and cardiovascular risk profile through and interactive dashboard. The UCC is a self-declared LHS.

Since both examples are located within cardiology and patients and medical staff were mostly involved in the LUMC or the UMC Utrecht, these examples were chosen for the interviews.

In addition, stakeholders were asked to reflect on two initiatives currently used in the field of cardiology in the Netherlands, that were identified by the present study's researchers as examples of care practices moving toward the implementation of an LHS, specifically[1]: The Box,[12] and[2] the Utrecht Cardiovascular Cohort (UCC)[13] (see Table 2 for a detailed description).

The focus groups were conducted by two researchers (RvdG and MdV). Respondents were interviewed by one researcher (SL). Verbal informed consent was obtained from all respondents. Initial interview topics and questions were formulated after the examination of the relevant literature and discussion with all team members.

2.2.2 | Individual interviews

After the focus groups, 35 individual interviews were held with stakeholders. These interviews were conducted following a design similar to that of the focus groups. Respondents were approached purposefully from ethical review boards across the Netherlands. In addition, patients from the cardiology departments of the LUMC an the UMC Utrecht were recruited via research nurses. In the interviews, respondents were asked to reflect on the concept of an LHS. If they were unable to do so, the work definition was provided. If a respondent was still unable to reflect, the two examples used in the focus groups

TABLE 3 Topic list focus group interviews.

Topic
Introduction • Welcome • Informed consent • Introduction researchers and respondents • Start recording
1. LHS in general • Familiarity → short explanation LHS • Recognition—examples in practice • Initial thoughts • Implementation • Barriers for participation
2. Informed consent • Information provision • Approach
3. Ethical oversight • Ethical review • Responsibilities • Accountability
4. Patients in LHS • Patient participation—conditions for patient participation
Ending • Final thoughts • Thank you moment

were employed. Individual interviews lasted up to 60 minutes and were held in Dutch and English depending on the preference of the respondent.

The semi-structured interviews were conducted according to a predefined topic list; an overview of the topic list can be found in Appendix 1, Table 3. According to the technique of constant comparative analysis, the interview topics evolved as the interviews progressed through an iterative process where repeating rounds of analysis are performed until saturation is reached.

2.3 | Data analysis

Both the focusgroup interviews and the individual interviews were recorded and transcribed verbatim. After transcription, interviews were coded in Atlas.Ti version 7.01.04 using open coding as described by Corbin and Strauss.[14] Transcripts were anonymized and were checked for commonalities and differences in descriptions of relevant topics by three members of the research team (SL, RvdG, and MdV) to ensure objective coding. Appropriate provisions were made to protect the privacy and confidentiality of interviewees and the data.

2.3.1 | Focus groups

To increase the internal validity of interpretations of provided topic descriptions, the resulting codes and themes of all five focus groups were discussed via a process of journaling until an agreement was reached between three researchers (SL, RvdG, and MdV) on the most suitable codes and themes for each focus group. After this process of journaling, findings were reported to the complete research team and discussed further until satisfaction.

2.3.2 | Individual interviews

Next, the individual interviews were analyzed in Atlas.TI. A conceptual framework of the structure of the data were created after conducting one-third of all interviews. To increase external validity, the results were presented to an extra focus group of seven new stakeholder members in the last phase of data collection (member check), after two-third of the interviews was conducted. Subsequently, changes in the framework were made based on suggestions by this focus group, and the resulting topic list was adapted for the remaining one-third of interviews.

2.3.3 | Member check

After conducting the final interviews, another member check was held, where respondents had the opportunity to comment on a preliminary report of the present study.[15] The extra focus group consisted of three cardiologists, an ethicist, a patient and the partner of the patient, a health lawyer and a methodologist.

3 | RESULTS

Across the focus groups and individual interviews, saturation was reached on three different themes: ethical oversight issues[1] patient engagement[2] and the patient as quantified self.[3]

Since The Box and the UCC were used as examples, respondents expressed their opinions and attitudes toward these systems. Therefore, some of our findings are specifically for these examples. When findings or quotes are on The Box or the UCC specifically, this is mentioned in the relevant results section.

3.1 | Ethical oversight issues

Various stakeholders described several ethical oversight issues when an LHS would be implemented on the cardiology department. These issues consisted of: informed consent, data ownership, data quality and learning culture. Anomynous quotes from the interviews can be found in Supplement 1.

3.1.1 | Informed consent

Respondents had differing views on how informed consent should be asked within a future LHS in the cardiology department. Ethicists and

health lawyers stated that for patients to be truly informed, every different research protocol implemented within the LHS should be shared with patients and informed consent should be asked once again. Informed consent should guarantee the safety of patients within the LHS and protect them from involuntary research participation according to these respondents. Methodologist and some cardiologists were afraid that by asking informed consent, research outcomes would be jeopardized. According to these respondents, many patients would not provide their consent and research findings would show bias and become invalid due to a misrepresentation of different types of patients within the LHS. These respondents preferred to not ask informed consent for the use of data within the LHS and only ask informed consent for research aims that would go beyond reusage of data. Some respondents proposed that patients should be informed upon entering the hospital about the LHS and would then be provided with the opportunity to opt-out of the LHS. These respondents were ethicists, nurses, some cardiologists and some patients.

Patients were also asked to share their opinions on informed consent for their participation within the LHS. Patients wish to be informed about how their data are used, how the data are stored, who will see the data within the hospital, whether their data are shared with third parties and research outcomes linked to the LHS. Patients varied in what they wanted to be asked to consent to. Most patients wanted to be asked to provide their informed consent once, upon entering the hospital. Especially when only existing hospital data were used within the LHS, most patients did not want to be asked for their informed consent for every research protocol. However, patients agreed that they did not want to participate within a full LHS: an LHS in which care and research are fully integrated and RCTs are part of research activities. Patients provided various reasons for this statement. They felt that by transforming the departments to full LHSs they would lose their privacy and lose the overview of what would happen with their data and they stated that a full LHSs could never be truly transparent.

3.1.2 | Data ownership

Respondents disagreed on the ownership of patient data. Most respondents stated that patient data belong to patients. The patient should decide what he or she wants to do with these data. Other respondents argued that medical data belong to the hospital or even to society, as medical examination and healthcare are paid for by society. The hospital should safeguard these data and prevent a data breach.

According to respondents, the question of ownership forms a challenge for LHSs, as this has implications for data usage. Different issues surrounding data usage were raised by respondents depending on the type of LHS they were describing. These issues consisted of[1]; data sharing with third parties (other [Dutch] hospitals, pharmaceutical companies, government bodies and insurance companies),[2] the sharing of incidental findings which are the result of research activities with patients, and[3] payment of data research. Respondents vary in their opinions on data sharing. Some stated that data, if anonymized, might be used by third parties, such as insurance companies and pharmaceutical companies. Others stated that only doctors should use medical data for research. The motivation for data sharing varied strongly based on their profession and opinions on ownership. Almost all respondents who were cardiologists, research nurses, insurance spokespersons and methodologists stated that data are needed for research and that scientific progress is significant. Data should, therefore, be shared and used and might even, according to some respondents, belong to the hospital. Ethicists and health lawyers, however, declared that patient data belongs to patients and should not be shared with third parties. Different respondents stated that there might be incidental findings from research activities within the LHS. They argued that a policy for these findings should be decided on before implementation. Few respondents argued that if patients are the owners of their data, they should share in profits if anything is gained from research with their data.

Data storage also forms a challenge to a future LHS in the cardiology department, since it demands a safe storage space and safe usage, according to some respondents. These respondents were cardiologists, methodologists and some were research nurses. Respondents varied in their opinions about the ability of hospitals to safeguard patient data for research purposes, especially when these would be used for both clinical care and research as they would be in an LHS. Some respondents stated that data can be safely stored and used within the LHS, others said that hospitals will never be able to completely ensure data safety.

3.1.3 | Data quality

Respondents, especially methodologists, wondered if data gathered within an LHS would be of the same quality as data gathered in more traditional research settings such as RTCs. While some respondents viewed RCTs as the golden standard for research, others viewed data gathered within the LHS as more "realistic" or as "a useful addition to data from RCT's." In addition, respondents asked questions on the generalizability of data outside of the LHS.

Different types of respondents wondered how data should be collected within a future LHS. Respondents stated that to ensure data validity, all data registrations of clinical care would have to be standardized within the LHS. This could, according to respondents, be problematic for clinical care, since personal details might become lost in such a system.

3.1.4 | Learning culture

Respondents, mainly cardiologists, mentioned that to achieve continuous learning, the cardiology department must establish a culture that actively promotes such learning. Such a culture can be established, according to respondents, through optimization of existing research

structures within the department, reusage of clinical data, and promoting open communication in which research is viewed as a team effort. Some respondents, for instance, pointed out that medical errors should be openly discussed within the team to optimize healthcare. In addition to establishing a culture of open communication, data usage should be optimized through synchronizing data infrastructures between systems and departments, so that collaborations with other departments and hospitals or even general practitioners might be possible.

Respondents also mentioned potential pitfalls of the LHS with regard to learning culture. For instance, some respondents were afraid that by implementing the LHS, doctors and other healthcare professionals might be tempted to mindlessly follow advice and directions formulated by algorithms of the LHS. Various respondents suggested that this could lead to a loss of tacit knowledge. The medical knowledge and intuition healthcare practitioners cultivate through their medical training and experience might lose intrinsic value when medical processes and decisions are guided by automated systems. New technology is, according to some of the interviewed ethicists, not neutral and could influence both healthcare practitioners and patients. When a cardiology department transitions toward an LHS, the effects of this transition on patients and healthcare workers should be monitored, according to these ethicists.

3.2 | Patient involvement within the LHS

According to several different stakeholders, patients have a unique position within the LHS. Three different kinds of patient involvement that would occur within an LHS as it is implemented in a cardiology department were identified.

3.2.1 | Insights into one's health

First, respondents said that patients within an LHS will be able to monitor their health, if the system is appropriately designed. As a result, patients will learn more about their medical condition, increasing so called "patient education," when compared to a non-LHS healthcare system. Concerning The Box, respondents stated that patients could, for example, learn more about their health status via home monitoring by e-health devices and through interactive online dashboards. So if an LHS such as The Box, is designed to gather data for research purposes, such data can also be used to implement personalized medicine for patients. Patients stated that personal information is helpful for their physical and mental healing process.

3.2.2 | Determining the goals of the LHS

According to the respondents, patients should help to determine the goals of an LHS. This could be done using input from patient organizations or patient member boards. Within an LHS, patients might also provide doctors and researchers with their ideas for research, according to most respondents. Especially the interviewed patients, nurses and ethicists acknowledged the role of patients as essential in determining the research agenda.

Patients within an LHS could, according to several respondents, also be invited to provide healthcare staff with feedback on the care they received. According to these respondents, the LHS forms a novel approach to the provision-of-care-feedback, one that goes above and beyond current feedback processes in healthcare.

3.2.3 | Altruism and willingness to participate

Respondents were asked if patients have a moral obligation to participate in an LHS. Some patient respondents articulated that they indeed felt this moral duty and were willing to help the next generation of patients by participating and actively promoting an LHS.

Other, non-patient respondents did not recognize patient participation in the LHS as a moral duty. They stated that patients might have a duty to share their data for quality improvement goals, but patients do not have a moral obligation to participate in an LHS within the cardiology department.

3.2.4 | Prepositions for patient engagement in the LHS

Respondents named several conditions that should be taken into consideration before patients participate actively within an LHS. First, patients should, according to various respondents, profit form their efforts.

Patient respondents pointed out that before they are willing to share their medical information with a department or researcher, a relationship built on trust must be established. To achieve such a relationship, clear communication is needed. Patient respondents pointed out that they want to know who might see the data, what their data will be used for, and mentioned that they wish to be informed about research output. At the moment, not all processes at the cardiology departments that were defined as LHSs by the researchers provide useful personal health feedback to patients, according to respondents familiar with the concept. To enable patients to learn about their health within an LHS, it is crucial that devices and interfaces work reliably, and technical support is available.

Next to clear communication, patients should, according to respondents, be educated about the goals of research, within the context of an LHS. Active participation within the LHS might, according to some non-patient respondents, not be an option for all patients, but according to most respondents, the hospital or cardiology department should invest in clear patient communication and education to implement an LHS that promotes patient engagement.

3.3 | The patient as a quantified entity within the LHS

3.3.1 | Quantified self

Respondents stated that an LHS is built with quantified patient information. Measurements such as blood pressure, use of medication and other quantified data are needed to perform research within the LHS. Some respondents were afraid that this might lead to a loss of personalization or individualized care.

Other respondents reported fearing that patients may have to perform more measurements when the cardiology department becomes an LHS. Participating ethicists, patients and various research nurses identified several effects of multiple repeated measurements that patients must perform at home. Patients might experience stress when their data hints toward bad health or when devices are not working sufficiently, according to these respondents. They further suggested that not all patients might be able to perform the required measurements and might, therefore, be excluded from participating in e-health practices. Measurements are multi-interpretable and may vary based on the moment of measurement or due to external influences. Therefore, healthcare workers are trained to read these measurements and look for trends. Patients miss, according to respondents, sufficient training to interpret outcomes. On top of that, patients might be frequently confronted with their illness and status as a sick person when they are continuously asked to perform measurements, according to several respondents.

While insight into one's healthcare data might motivate patients pursue healthier behavior, some respondents argued that by being given feedback about their health, patients experience a loss of freedom. They explained that providing feedback, for instance through health monitoring, creates an obligation for the patient to maintain a healthier lifestyle. Being healthy and striving toward a healthy and responsible lifestyle could become the most important value of the LHS, according to these respondents.

Other respondents claimed that when patients wish to adopt a different lifestyle, the LHS might provide the data patients need to do so and give patients feelings of control and safety. This was true for some patient respondents who used The Box.

According to some respondents, gathering data for research in a future LHS poses no risks to patients when the data that is gathered is part of standard care. These respondents did not recognize the risk of the quantified self. These respondents were cardiologists and some methodologists. Patients did not describe this view in any of the interviews.

3.3.2 | Role for qualitative data

According to some respondents, the effects of repeated measurements within the LHS could be solved by also incorporating qualitative data in the LHS. Patients, as well as healthcare workers, should be encouraged to share their stories, according to these respondents. This will allow for a more individual approach to healthcare and research.

4 | DISCUSSION

We studied stakeholders' perspectives on the ethical issues when an LHS is implemented within a cardiology department. Our results show that while the LHS is a relatively new topic, many respondents have opinions regarding various aspects of implementation of a (future) LHS. These opinions express hopes and concerns for the knowledge an LHS is able to generate, but also involve the quantification of patients and accountability for processes and outcomes of the LHS. Respondents suggested that when an LHS is implemented, the goals of such a system must be made clear to ensure an ethical transition from (regular) clinical care toward an LHS. In addition, respondents were optimistic about the potential of an LHS to lead to greater patient engagement in both medical research and clinical care, allowing patients to provide their input on research themes and learn more about their own disease.

Our respondents described two important themes regarding the role of patients in LHSs: quantification of patients and patient engagement. Quantification of patients occurs when patients are asked to participate in an LHS through usage of their medical data. This quantification was described by our respondents as positive and negative; it could lead to a better understanding of one's health, but it could also make patients feel quantified. This is described in the literature as the quantified self; striving toward the quantification of a person by gathering and analyzing information about oneself to optimize oneself (eg, behavior and health).[16] While this quantification can allow for optimization of the self, empowerment of patients and greater self-knowledge,[17] various philosophers and researchers have warned for negative side effects of this movement, including the loss of privacy, feelings of restlessness and responsibility for one's own health and the disruption of data sciences since individuals all generate their data in themselves.[18,19] These negative effects have yet to be solved when an LHS is implemented within cardiology.

A future LHS can be promising for cardiology patients since the LHS can be employed to enlarge or promote patient engagement. Patients can help to determine research agendas and quality goals beyond the use of patient reported outcomes. Faden and colleagues, amongst others, have argued that patients have a moral obligation to participate in LHSs.[11] They describe that patients should not be asked for their informed consent for some learning activities within the LHS. Especially activities that make use of patient data should only be reviewed by an ethics committee, the Institutional Review Board (IRB) in the United States.[11] This view is not shared by our patient stakeholders; patients expressed that they wanted to be informed about oversight measures and some said that they did not want to share their data within a future LHS. They want to give their informed consent for data usage. Only some patients expressed that they did not care about providing their consent for the usage of their data. Our study shows that patients desire an active role within LHSs and the

cardiology department. Informed consent for data sharing and other research activities within a future LHS should be designed specifically to benefit both researchers and patients; researchers should be able to perform research within a future LHS without being unnecessarily hindered and patients should be included in the research by giving consent for the usage of their data. However, more research is needed to investigate how patient engagement can be employed within a future LHS and how ethical concerns concerning this engagement can be solved.

Different concerns expressed by stakeholders are also present in discussions on LHSs in the (scientific) literature. Various authors have argued that knowledge generated within an LHS might not be of the same value as the knowledge generated in more traditional research settings. Data collected within an LHS will often be observational, meaning it will encounter the same methodological problems as any type of observational study, for example, knowledge generated from LHS may suffer from confounding that needs accounting for.[20] In addition, electronic health records, which will be the main data source in LHS, are known to harbor lower quality data than data that is purposely and prospectively collected in a clinical study like an RCT.[21] However, respondents varied in how they viewed the value of observational data from the LHS. Some of our stakeholders argued that observational data generated within and LHS can be seen as valuable since it adds to knowledge generated in trial settings. More epidemiological research on the exact value of observational data in an LHS and methods for the generation of knowledge from the LHS is highly needed.

Strengths of this study include the variety of the respondents that were included in our focus groups and individual interviews. By asking all stakeholders that may be involved in a future LHS in cardiology, a more complete overview of ethical issues that could arise upon implementation was given. In addition, one of the strengths of this study is the voice of the patients on examples from their daily practices as cardiology patients and their involvement in both the UCC and The Box. Earlier research used hypothetical cases to study patients' perspectives.

Limitations include the limited ability of some of the respondents to reflect on the LHS as a concept. While some respondents had previous work experience with LHSs, others were only able to reflect on parts of the LHSs. This entails that some respondents were only able to answer our questions when we provided the working definition or were only able to reflect on The Box or The UCC. They were unable to provide insides on other examples of LHSs. While some were less familiar with the concept, others expressed that they viewed the term "LHS" as a buzzword for practices that combine clinical care and research that they were implementing already. Respondents were therefore struggling with the exact meaning of the concept of an LHS, which lead to different views and goals for the LHS and ideas on how to move forward. This is also visible in literature as different studies on the LHS show that there are various opinions on what an LHS is and how it should be managed in an ethical fashion.[22,23]

In summary, this qualitative study, using semi-structured and focus group interviews to identify ethical challenges of an LHS in cardiology, found that relevant stakeholders are convinced that when an LHS is implemented, it can help to provide a higher quality of care, make research easier and can be employed as a tool to engage patients when ethical obstacles such as the quantification of patients can be overcome.

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DATA AVAILABILITY STATEMENT

The data underlying this article cannot be shared publicly due the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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